Cornell University
College of Veterinary Medicine

Dr. Paula Cohen wins Gates grant for her new take on male contraception

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In time, men may have a new way to prevent pregnancy, thanks to the innovative thinking of a Cornell geneticist.

Paula Cohen, professor of genetics in the College of Veterinary Medicine, has won a $100,000 grant from the Bill & Melinda Gates Foundation to develop a radical approach to contraception – an area that has remained static for many

years.

“That’s what’s truly innovative here: We are targeting a stage in the reproductive cycle that’s poorly understood,” Cohen said.

An expert in the genetics of fertility, Cohen was one of 28 researchers, chosen from 1,600 applicants from around the world, awarded a Grand Challenges Explorations grant, funded by the Gates Foundation. The grant supports innovative thinkers worldwide to explore ideas that can break the mold in how we solve persistent global health and development challenges. Successful projects have the opportunity to receive a follow-on grant of up to $1 million.

Cohen’s project will look at meiosis, a poorly understood stage of development in which a sperm cell’s DNA is halved. When the sperm fertilizes an egg – which also contains only one half of its chromosomes – the resulting embryo is restored to the full number of chromosomes.

“I’ve always thought that if we can stop those cells from actually getting into meiosis, you’d have a really good contraceptive,” Cohen said.

There are several reasons why this stage of sperm cell development is a better target for contraception than others, she said.

Traditionally, contraceptives have tried to block the sperm from getting to the egg, with barriers like condoms and spermicide. “That’s shutting the stable door after the horse has bolted,” Cohen said. “If a single swimmer gets out, it still has the potential to fertilize an egg, and you can’t always prevent that from happening.”

Hormonal approaches, like birth control pills, have their own drawbacks. Cohen believes they are not always good for women. And the development of a male birth control pill has always been scorned by men who fear that their libido and/or male sexual characteristics will be diminished.

And contraceptives that target the sperm cell in the testis at a late stage of development might result in mutant sperm and thus birth defects.

Her new approach, centering on the sperm cell’s entry into meiosis, before it even leaves the testis, offers several benefits.

For example, should one sperm sneak its way through to meiosis, the “surveillance machinery” present during meiosis would get rid of that solitary cell; in other words, the meiotic process itself would “check” for escapers. And unlike later stages of sperm cell development, the cell’s entry into meiosis is accessible to blood-borne factors such as drugs.

“The problem is, we know very little about meiosis, because it’s a very hard stage to target biologically or molecularly,” she said. “Only recently have we started to gather the tools to be able to look at it.” One tool Cohen will use is called CRISPR/Cas9, a genome editing technology that allows genes to be modified permanently and very rapidly.

She has three goals. First, she’ll try to prove she can get the sperm cells to go into meiosis in culture. Second, she’ll monitor the cells’ entry, by engineering what are known as reporter mice, whose cells turn green or red depending on whether or not they have entered meiosis. Third, and as proof-of-principle, she’ll try to manipulate two genes that are known to affect a cell’s entry into meiosis.

One gene is required for sperm stem cell maintenance in the testes; if it is deleted, cells rapidly progress into meiosis. The second gene is required for the sperm cell to enter meiosis; it if is blocked, the cells stop developing. “So we’ve got a gene that should accelerate their entry into meiosis and one that should slow it down,” Cohen said.

If she can manipulate those genes, that opens the door to the possibility of finding others. “There could be hundreds of genes that control this process,” she said. “We just need to find them and begin to ask whether they are potential contraceptive targets.”

This is not the type of science that would qualify for funding through traditional agencies like the National Institutes of Health, Cohen said.

“It’s very out there, it’s very risky, and that’s what the Gates Foundation is going for,” she said. “They want you to come up with ideas that are truly revolutionary.”

By Susan Kelley

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